REMARKS

On entry of the following amendments, claims 20, 22, and 26-34 are currently pending. Claims 1-19 and 23-25 were previously cancelled. Claim 21 is cancelled herein. Claims 20-22 and 26-32 currently stand rejected. Claims 33 and 34 are newly added. Claims 20, 22, 31, and 32 are amended herein.

Summary of Telephonic Interview

Applicants appreciate the time and attention of Examiners Shirley Gembeh and Robert Hayes during the telephonic interview of January 7, 2010. During the interview, the outstanding written description and enablement rejections based on 35 U.S.C. 112, first paragraph were discussed.

Specifically, **agreement was reached** that amending claim 20 so that "R^1 is H, unsubstituted or substituted straight or branched alkyl" would overcome the outstanding written description rejection, and Applicants have amended claim 20 accordingly.

Regarding the enablement rejection, the Examiner made suggestions as to clarifying amendments for claim 20, and Applicants have amended this claim in conformity with these suggestions. Applicants respectfully request the Office consider these amendments in light of the remarks below.

Amendments to the Claims

Applicants have amended claim 20, to improve clarity and to more clearly and distinctly point out the subject matter claimed. Specifically, Applicants have amended the variable R^1, deleted many of the recited indications, rearranged the wording of the claims so that the remaining indications are listed at the beginning of the claim, and specified that the claimed method treats a mammal. Applicants have also moved some of the other features of the claims to newly added dependent claims 33 and 34. As a result, Applicants have cancelled claim 21 and have amended claims 22, 31 and 32 to correct antecedent bases.

These amendments do not add new matter. Applicants hereby reserve the right to pursue any deleted subject matter in one or more continuing applications.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Office will be addressed below in the order they appear in and using the enumeration from the prior Office Action.

5. Withdrawal of Prior Rejections of Record

Applicants note with appreciation the withdrawal of the prior obviousness-type double patenting rejection over claims 17-34 of U.S. 7,148,239.

6. Rejection Based on 35 U.S.C. § 112, Second Paragraph - Claim 20

Claim 20 is rejected under 35 U.S.C. § 112, second paragraph for **indefiniteness** for lack of antecedent basis in claim 22. Applicants have amended claim 22 to correct this inadvertent error and request reconsideration.

7. Rejection Based on 35 U.S.C. § 112, First Paragraph – Claim 20-22, 26-29 and 31-32

Claims 20-22, 26-29 and 31-32 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the **written description** requirement. Specifically, the Office contends that the claims contain subject matter which was not described in the specification to reasonably convey to one of skill in the art that the inventors had possession of the claimed invention. Applicants respectfully traverse the rejection to the extent that it is maintained over the claims as currently amended.

The Office appears to take issue with the number of examples disclosed by Applicants, stating that "[t]he mere fact that Applicant may have discovered one type of derivative of the compound of formula I to be effective ... is not sufficient to claim the entire genus of the compound of formula I." Office Action dated July 21, 2009 at 4 (emphasis added). The Office notes that written description may be satisfied by "disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties" and that "disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure 'indicates that the patentee has invented species sufficient to constitute the gen[us].'" *Id.* at 4-5 (emphasis added).

Applicants respectfully assert that they have satisfied the standard presented by the Office. In particular, regarding claim 30, which covers a method of using the compound 5,6-dihydro-5-(1-piperidinyl)-methyl-3-(3-pyridyl)-4*H*-1,2,4-oxadiziane ("iroxanadine"), Applicants have exemplified this compound in Example 64 of the specification and tested this compound in a variety of assays and reported these results in Tables 2-5. Considering their disclosure of the preparation of this compound and its biological activity in the original application, Applicants have undoubtedly shown that they were in possession of the scope of the invention embodied by claim 30.

Claim 20 as amended herein is a relatively narrow genus encompassing the compound iroxanadine of claim 30. In exemplifying iroxanadine, Applicants have demonstrated possession of a species "sufficient to constitute [a] genus," i.e., sufficient to constitute a limited genus of compounds with structural similarity to iroxanadine. Claim 20 recites only three variables (A, R^1, and R"), each of which is limited to only a few possibilities, particularly after accounting for the present amendments to variable R^1. Applicants have disclosed the "relevant, identifying characteristics, [such as chemical] structure" by disclosing iroxanadine and its core structure, and the genus around iroxanadine shares these relevant structural features without any major deviations. Additionally, as indicated in paragraph 0077 of the published original application, compounds of formula I" are cyclic forms of compounds of formula I, and so exemplification of the wide range of variables for formula I (see other Examples in the specification) supports exemplification for corresponding variables in formula I", particularly because in certain instances these compounds may interconvert via tautomerization.

For at least these reasons, one of skill in the art would have appreciated that Applicants had possession of the invention recited in claim 20 as amended herein. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

8. Rejection Based on 35 U.S.C. § 112, First Paragraph – Claim 20-22 and 26-32

Claims 20-22 and 26-32 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the **enablement** requirement. Specifically, the Office contends that the claims encompass subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or

use the invention. Applicants respectfully traverse this rejection to the extent that it is maintained over the claims as amended herein.

As an initial point, Applicants have amended claim 20 to recite a more limited set of indications. In particular, Applicants have amended this claim to recite cardiovascular indications (e.g., atherosclerosis, coronarial disease, and pulmonary hypertonia - see paragraph 0145 of the published application), ischemic diseases (e.g., cerebrovascular ischemia, stroke, and traumatic head injury – see paragraph 0146 of the published application), as well as the epithelial diseases of renal tubules. The numerous experimental data in the original application fully support enablement for the treatment of these indications. For example, the various experiments associated with paragraphs 0600, 0626, 0657, 0770 and 0788 involve cells from different heart systems and demonstrate the applicability of the subject method in cardiovascular indications. Similarly, the experiments of paragraphs 0626, 0654-0657 and 0792 test the ability of various cells to handle ischemic stresses and support use of the subject compounds in ischemic indications. Lastly, the experiments detailed in paragraphs 0817 and 0831 employ epithelial cells and evince the utility of the present compounds in epithelial indications, such as epithelial disease of renal tubules. Accordingly, Applicants submit that claim 20 as amended herein is fully enabled by the original disclosure.

Applicants also highlight that the indications recited in claim 20 as amended are all well-known and understood by one of skill in the art. Importantly, one of ordinary skill in the art would readily be able to identify the patient population to be treated using routine and known methods. It is Applicants' method of treatment that is a novel and non-obvious advance over the art.

Regarding the particular points raised by the Office in the outstanding Action, the Office submits that "none of the diseases are related and none of the diseases appear to be due to a dysfunction of any generic compound recited in the claims." *Id.* at 6. While Applicants are unsure as to the meaning of the last part of this statement and request clarification if the rejection is to be maintained, Applicants nonetheless point out that the diseases recited in claim 20 as amended herein are related, for example, by being cardiovascular indications or ischemic indications (or both), or epithelial disease of renal tubules, which all share the common feature of being related to epithelial cell functions.

While the Office submits that the recited diseases have different "etiologies," *Id.* at 9, 10, Applicants respectfully point out that the causes of the diseases are irrelevant. Rather, in this case, it is the effect of the diseases that is dispositive, and the effect of the recited diseases, the stress or injury to the cells of the mammal, is the point at which the subject compounds are effective in treatment. For example, as Applicants have noted previously, "Exhibit B illustrates that cancer (a neoplastic disease) and Creutzfeldt-Jakob disease (an infectious disease caused by abnormal proteins called prions), completely unrelated diseases, nonetheless share an involvement in defective protein folding that may be affected by expression of a molecular chaperone." Applicants' Office Action Reply dated December 11, 2008 at 6. While cancer and Creutzfeld-Jakob disease, for example, plainly have different etiologies, they can produce similar stresses and injuries to cells, and at this point the subject compounds can be effective.

The Office also appears to conclude that identification of "which chaperone system is affected" is necessary and that this identification requires undue experimentation. Applicants respectfully disagree, and submit, as they have previously, that heat shock proteins are a class of molecular chaperones that are pervasive in the cellular response to stresses and injuries. *Id.* Hence, the experiments described in the instant application, which the Office has acknowledged demonstrate the effectiveness of the subject compounds in generating a heat shock response, are generally applicable to molecular chaperone systems and thus individual identification is not necessary.

In support of the enablement rejection, the Office cites as an example that " treatment of viral disease, bacteria, tumor and immune disease alone is cumbersome." Office Action dated July 21, 2009 at 7. Although Applicants disagree, as noted above, Applicants have amended claim 20 to no longer recite these particular indications and hence assert that this claim is enabled for the indications presently recited.

For at least the above reasons, Applicants submit that claim 20 as amended is enabled by the original specification and request reconsideration and withdrawal of the rejection.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 212.596.9000. Any other fee required for timely consideration of this submission may be charged to Deposit Account No. 06-1075, under Order No. 004049-0015-103 from which the undersigned is authorized to draw.

Dated: January 21, 2010

Respectfully submitted,

By_____

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